WHAT IS CLAIMED IS:

- 1 1. An isolated DNA molecule selected from the group consisting of:
- 2 A. the DNA sequence of FIGURE 1 (SEQ ID NO:1);
- B. the DNA sequence of FIGURE 2 (SEQ ID NO:3);
- 4 C. the DNA sequence of FIGURE 20A (SEQ ID NO:22);
- D. DNA sequences that hybridize to any of the foregoing DNA
- 6 sequences under standard hybridization conditions;
- 7 E. DNA sequences that code on expression for an amino acid sequence 8 encoded by any of the foregoing DNA sequences;
- 9 F. degenerate variants thereof;
- 10 G. alleles thereof; and
- 11 H. hybridizable fragments thereof.
 - 1 2. An isolated nucleic acid molecule, which nucleic acid molecule encodes an
 - 2 ob polypeptide, which polypeptide is characterized by having about 145 to about
 - 3 167 amino acid residues, being expressed predominantly by adipocytes, and being
 - 4 capable of inducing a reduction of body weight in an animal.
 - 1 3. The isolated nucleic acid of Claim 2, wherein the ob polypeptide has an
 - 2 amino acid sequence selected from the group consisting of the sequence depicted
- 3 in Figure 1 (SEQ ID NO:2), Figure 1/from amino acid number 22 to amino acid
- 4 number 167, Figure 3 (SEQ ID NO:4) Figure 3 from amino acid number 22 to
- 5 amino acid number 167, Figure 5 (SEQ ID NO:5), Figure 5 from amino acid
- 6 number 22 to amino acid number 166, Figure 6 (SEQ ID NO:6), and Figure 6
- 7 from amino acid number 22 to amino acid number 166.
- 1 4. The nucleic acid molecule of Claim 2 selected from the group consisting of
- 2 DNA and RNA.

- 1 5. The nucleic acid molecule of Claim 2, which has a sequence as shown in
- 2 Figure 1 (SEQ ID NO:) from nucleotide number 46 to nucleotide number 550.
- 1 6. The nucleic acid molecule of Claim 2, which has a sequence as shown in
- 2 Figure 2 (SEQ ID NO:2) from nucleotide number 46 to nucleotide number 550.
- 1 7. The nucleic acid mplecule of Claim 1 which is detectably labeled.
- 1 8. A cloning vector, which comprises the DNA molecule of Claim 1.
- 1 9. An expression vector, which comprises the nucleic acid molecule of Claim
- 2 2, operatively associated with an expression control sequence.
- 1 10. The expression vector of Claim 9, wherein said expression control
- 2 sequence is selected from the group equisiting of the cytomegalovirus hCMV
- 3 immediate early gene, the early of late promoters of SV40 or adenovirus, the <u>lac</u>
- 4 system, the <u>trp</u> system, the <u>TAC</u> system, the <u>TRC</u> system, the major operator and
- 5 promoter regions of phage λ , the control regions of fd coat protein, the promoter
- 6 for 3-phosphoglycerate kinase, the promoters of acid phosphatase, and the
- 7 promoters of the yeast α -mating factors.
- 1 11. A probe capable of screening for a nucleic acid encoding an ob polypeptide
- 2 in alternate species, which probe is a labeled DNA molecule of Claim 1.
- 1 12. A unicellular host transfected with a cloning vector of Claim 8.
- 1 13. A unicellular host transfected with an expression vector of Claim 9.
- 1 14. The unicellular host of Claim 13 wherein the unicellular host is selected
- 2 from the group consisting of E. coli, Pseudomonas, Bacillus, Streptomyces, Pichia

- 3 yeasts, CHO, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, and BMT10 cells,
- 4 plant cells, insect cells, and human cells in tissue culture.
- 1 15. An oligonucleotide primer for amplifying human genomic DNA encoding
- 2 an ob polypeptide.
- 1 16. The oligonucleotide of Claim 15, which is selected from the group
- 2 consisting of
- 3 HOB 1gF 5'-CCCAAGAAGCCCATCCTG-3' (SEQ ID NO:26)
- 4 HOB 1gR 5'-GACTATCTGGGTCCAGTGCC-3' (SEQ ID NO:27)
- 5 HOB 2gF 5'-CCACATGCTGAGCACTTGTT-3' (SEQ ID NO:28)
- 6 HOB 2gR 5'-CTTCAATCCTGGAGATACCTGG-3' (SEQ ID NO:29).
- 1 17. An ob polypeptide, which polypeptide is encoded by the DNA molecule of
- 2 Claim 1.
- 1 18. An ob polypeptide, which polypeptide is characterized by having about 145
- 2 to about 167 amino acid residues, being expressed predominantly by adipocytes,
- 3 and being capable of inducing a reduction of body weight in an animal.
- 1 19. The ob polypeptide of Claim 18 which has the amino acid sequence shown
- 2 in Figure 1 (SEQ ID NO:2) or Figure 5 (SEQ ID NO:5).
- 1 20. The ob polypeptide of Claim 19 which has the amino acid sequence shown
- 2 in Figure 3 (SEQ ID NO:4) or Figure 6 (SEQ ID NO:6).
- 1 21. An immunogenic fragment of an ob polypeptide, which polypeptide is
- 2 characterized by having about 160 amino acid residues, being expressed
- 3 predominantly by adipocytes, and being capable of inducing a reduction of body
- 4 weight in an animal.

- 1 22. The immunogenic fragment of an ob polypeptide of Claim 21, which is
- 2 selected from the group consisting of
- 3 Val-Pro-Ile-Gln-Lys-Val-Gln-Asp-Asp-Thr-Lys-Thr-Leu-Ile-Lys-Thr (SEQ
- 4 ID NO:18);
- 5 Leu-His-Pro-Ile-Leu-Ser-Leu-Ser-Lys-Met-Asp-Gln-Thr-Leu-Ala (SEQ ID
- 6 NO:19);
- 7 Ser-Lys-Ser-Cys-Ser-Leu-Pro-Gln-Thr-Ser-Gly-Leu-Gln-Lys-Pro-Glu-Ser-
- 8 Leu-Asp (SEQ ID NO:20); and
- 9 Ser-Arg-Leu-Gln-Gly-Ser-Leu-Gln-Asp-Ile-Leu-Gln-Gln-Leu-Asp-Val-Ser-
- 10 Pro-Glu-Cys (SEQ ID NO:21).
- 1 23. A method for preparing an ob polypeptide comprising:
- 2 A. culturing a unicellular host of Claim 12 or 13 under conditions that
- 3 provide for expression of the ob polypeptide; and
- B. recovering the expressed ob polypeptide.
- 5 24. The method according to Claim 23 wherein the host cell is a bacterium.
- 1 25. The method according to Claim 23, wherein the host cell is a yeast.
- 1 26. The method according to Claim 23, further comprising:
- 2 C. chromatographing the polypeptide on a Ni-chelation column; and
- 3 D. purifying the polypeptide by gel filtration.
- 1 27. The method according to Claim 26, further comprising after step C and
- 2 before step D chromatographing the ob polypeptide on a strong cation exchanger
- 3 column.
- 1 28. An antibody to the ob polypeptide of Claim 17.
- 1 29. An antibody to the ob polypeptide of Claim 18.

- 1 30. A method for preparing an antibody to an ob polypeptide, comprising:
- 2 A. conjugating the immunogenic fragment of an ob polypeptide of
- 3 Claim 19 to a carrier protein;
- B. immunizing a host animal with the ob polypeptide fragment-carrier
- 5 protein conjugate of step A admixed with an adjuvant; and
- 6 C. obtaining antibody from the immunized host animal.
- 1 31. An antibody to an ob polypeptide prepared according to a method
- 2 comprising:
- 3 A. conjugating an immunogenic fragment of an ob polypeptide of
- 4 Claim 19 to a carrier protein;
- 5 B. immunizing a host animal with the ob polypeptide fragment-carrier
- 6 protein conjugate of step A admixed with an adjuvant; and
- 7 C. obtaining antibody from the immunized host animal.
- 1 32. The antibody of Claim 28, 29, or 31 comprising a polyclonal antibody.
- 1 33. The antibody of Claim 28, 29, or 30 comprising a monoclonal antibody.
- 1 34. An immortal cell line that produces a monoclonal antibody according to
- 2 Claim 33.
- 1 35. The antibody of Claim 28, 29, or 31 labeled with a detectable label.
- 1 36. The antibody of Claim 35 wherein the label is selected from the group
- 2 consisting of enzymes, chemicals which fluoresce, and radioactive elements.
- 1 37. A method for measuring the presence of an ob polypeptide in a sample,
- 2 comprising:
- 3 A. contacting a sample suspected of containing an ob polypeptide with
- 4 an antibody that binds to the ob polypeptide under conditions which allow for the



- 5 formation of reaction complexes comprising the antibody and the ob polypeptide,
- 6 B. detecting the formation of reaction complexes comprising the
- 7 antibody and ob polypeptide in the sample;
- 8 in which detection of the formation of reaction complexes indicates the presence of
- 9 ob polypeptide in the sample.
- 1 38. The method of Claim 37 in which the antibody is bound to a solid phase
- 2 support.
- 1 39. The method of Claim 38 which further comprises contacting the sample
- 2 with a labelled ob polypeptide step (A), and removing unbound substances prior to
- 3 step (B), and in which the formation of reaction complexes in the sample is
- 4 detected by observing a decrease in the amount of labelled ob polypeptide in the
- 5 sample.
- 1 40. The method of Claim 38 which further comprises contacting the sample
- 2 with a labelled antibody in step (A), which labelled antibody is an anti-ob
- 3 polypeptide antibody, and removing unbound substances prior to step (B), and in
- 4 which the formation of reaction complexes in the sample is detected by observing
- 5 an increase in the amount of labelled antibody in the sample.
- 1 41. The method of Claim 37 in which an ob polypeptide is bound to a solid
- 2 phase support.
- 1 42. The method of Claim 41 which further comprises contacting the sample
- 2 with an ob polypeptide in step (A), and removing unbound substances prior to step
- 3 (B), and in which the antibody is labelled and the formation of reaction complexes
- 4 in the sample is detected by observing a decrease in the amount of labelled
- 5 antibody.

- 1 43. A method for evaluating the level of ob polypeptide in a biological sample 2 comprising
- A. detecting the formation of reaction complexes in a biological sample according to the method of Claim 30; and
- B. evaluating the amount of reaction complexes formed, which amount of reaction complexes corresponds to the level of ob polypeptide in the biological sample.
- 1 44. A method for detecting or diagnosing the presence of a disease associated 2 with elevated or decreased levels of ob polypeptide in a mammalian subject 3 comprising:
- A. evaluating the level of ob polypeptide in a biological sample from a mammalian subject according to Claim 43; and
- B. comparing the level detected in step (A) to a level of ob polypeptide present in normals or in the subject at an earlier time;
- 8 in which an increase in the level of ob polypeptide as compared to normal levels
- 9 indicates a disease associated with elevated levels of ob polypeptide, and decreased
- 10 level of ob polypeptide as compared to normal levels indicates a disease associated
- 11 with decreased levels of ob polypeptide.
- 1 45. A method for monitoring a therapeutic treatment of a disease associated
- 2 with elevated or decreased levels of ob polypeptide in a mammalian subject
- 3 comprising evaluating the levels of ob polypeptide in a series of biological samples
- 4 obtained at different time points from a mammalian subject undergoing a
- 5 therapeutic treatment for a disease associated with elevated or decreased levels of
- 6 ob polypeptide according to the method of Claim 43.
- 1 46. The method according to Claim 44 or 45, wherein the disease associated
- 2 with elevated levels of ob polypeptide is selected from the group consisting of
- 3 AIDS, cachexia, cancer, and anorexia nervosa.

- 1 47. The method according to Claim 44 or 45, wherein the disease associated
- 2 with decreased levels of ob polypeptide is selected from the group consisting of
- 3 obesity, Type II diabetes, hypertension, and elevated blood lipids.
- 1 48. A test kit for measuring the presence or amount of ob polypeptide in a
- 2 sample, comprising:
- A. an anti-ob polypeptide antibody of Claim 28, 29, or 30;
- B. means for detecting binding of the anti-ob polypeptide antibody to
- 5 ob polypeptide in a sample;
- 6 C. other reagents; and
- 7 D. directions for use of the kit.
- 1 49. A method for changing the body weight of a mammal comprising inhibiting
- 2 the expression of an ob polypeptide encoded by a nucleic acid of Claim 2.
- 1 50. The method according to Claim 49 comprising expressing an antisense
- 2 nucleic acid molecule hybridizable to a nucleic acid that expresses the ob
- 3 polypeptide, expressing a ribozyme that cleaves a nucleic acid that expresses the
- 4 ob polypeptide, administering an antisense nucleic acid molecule hybridizable to a
- 5 nucleic acid that expresses the ob polypeptide, and administering a ribozyme that
- 6 cleaves a nucleic acid that expresses the ob polypeptide.
- 1 51. A pharmaceutical composition for reducing body weight of an animal
- 2 comprising the ob polypeptide of Claim 17 and a pharmaceutically acceptable
- 3 carrier.
- 1 52. A pharmaceutical composition for reducing body weight of an animal
- 2 comprising the ob polypeptide of Claim 18 and a pharmaceutically acceptable
- 3 carrier.

- 1 53. A method for reducing the body weight of an animal comprising
- 2 administering an amount of a pharmaceutical composition of Claim 52 effective to
- 3 reduce the body weight of an animal to an animal believed to be in need of
- 4 decreased body weight.
- 1 54. The method according to Claim 53 wherein the animal is a human, and the
- 2 ob polypeptide is human ob polypeptide.
- 1 55. A method for reducing the body weight of a mammal comprising increasing
- 2 the expression of a protein encoded by the nucleic acid of Claim 2.
- 1 56. A pharmaceutical composition for increasing the body weight of an animal
- 2 comprising an antagonist of an ob polypeptide.
- 1 57. The pharmaceutical composition of Claim 56, wherein the antagonist is
- 2 selected from the group consisting of an antibody that binds to and neutralizes the
- 3 activity of ob polypeptide, a fragment of the ob polypeptide that binds to but does
- 4 not activate the ob receptor, and a small molecule antagonist of the ob
- 5 polypeptide.
- 1 58. A method for increasing the body weight of an animal comprising
- 2 administering an amount of the pharmaceutical composition of Claim 56 effective
- 3 to cause an increase in body weight to an animal believed to be in need of
- 4 increased body weight.

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